

**IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA**

**BIOGEN INTERNATIONAL GMBH
and BIOGEN MA INC.,**

Plaintiffs,

v.

MYLAN PHARMACEUTICALS INC.,

Defendant.

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) **C.A. No. 17-116-IMK**
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BIOGEN'S RESPONSIVE POST-TRIAL BRIEF

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Table of Abbreviations

MS	Multiple sclerosis
'514 patent	U.S. Patent No. 8,399,514
DMF	Dimethyl fumarate
JTX	Joint Trial Exhibit
DTX	Mylan Trial Exhibit
PTX	Biogen Trial Exhibit
PDX	Biogen Trial Demonstrative
Mylan Br.	Post-Trial Brief for Mylan Pharmaceuticals Inc. (D.I. 376)
[name] A:B	Trial testimony of [name] at page:line(s)

I. INTRODUCTION

Biogen submits this brief in response to Mylan's opening post-trial brief.

Mylan's sole claim at trial, on which it had the burden of proof by clear and convincing evidence, was that Biogen's U.S. Patent No. 8,399,514 ("the '514 patent") (JTX2000) lacks written description support under 35 U.S.C. § 112 for the subject matter of the asserted patent claims. Mylan failed to meet its burden. The '514 patent meets the written description requirement in full, and therefore judgment should be entered against Mylan.¹

The assessment of written description "requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* The written description requirement does not "demand either examples or an actual reduction to practice" demonstrating the inventor has tested the invention. *Id.* at 1352. Rather, "the hallmark of written description is disclosure." *Id.* at 1351. The test is met when the disclosure "allows one skilled in the art to visualize or recognize the identity of the subject matter purportedly described." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1308 (Fed. Cir. 2015) (quoting *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002)). The *Nuvo* case, on which Mylan relies, did not change these fundamental principles.

The '514 patent describes and claims innovative treatments for multiple sclerosis ("MS"), a chronic, progressing and debilitating disease. (*See, e.g.*, JTX2000 at 1:15-34.) The asserted patent claims cover Dr. Gilmore O'Neill's discovery, based on his insight into the pharmacology

¹ Mylan has stipulated to entry of judgment of infringement of each of the asserted claims of the '514 patent. (D.I. 288.)

of DMF, of a dose of 480 mg/day of DMF for the treatment of MS. (O'Neill 590:18-591:2.) Prior to Dr. O'Neill's discovery, the only medications available for MS were administered by injection. (JTX2133 at ¶ 10.) Dr. O'Neill's discovery led to the development of Tecfidera®, a highly effective oral therapy for the treatment of MS patients with 480 mg/day of DMF. (JTX2133 at ¶¶ 4-5 and 10-17; D.I. 376-1 at 10-11.)

As demonstrated at trial, the '514 patent specification (JTX2000) describes the claimed inventions, disclosing and linking the three elements set forth in each of the asserted claims: (1) a method of treating MS (2) with DMF and/or MMF (3) at a dose of 480 mg per day. The specification focuses on MS throughout as the disease targeted for treatment and describes methods for treating MS using DMF and/or MMF. The specification further discloses using DMF and/or MMF in an amount of 480 mg/day, identifying this dose as the lowest dose in the narrowest, most preferred range of disclosed doses and connecting it to the known effective dose of 720 mg/day.

In the Factual Background section below, Biogen briefly summarizes the trial evidence regarding the development of Tecfidera® and the prosecution of the '514 patent. The evidence at trial is substantially different from the account of events that Mylan states in its brief without record citation. Nowhere in the record, for example, is there evidence in support of Mylan's assertions, made without any record citation, that after the Phase III trials "Biogen found itself in a bind . . . [and] . . . began to engineer a wholesale transformation of [its] application" (Mylan Br. at 8) or that Biogen "completely rework[ed]" the application because a later patent application that Biogen had filed "faced long odds in a field crowded with prior art." (*Id.* at 1.) As discussed below, the '514 patent specification always included disclosure of the claimed inventions and was never "repurposed," and the patent claims were thoroughly examined by the Patent and Trademark

Office and deemed patentable.

II. FACTUAL BACKGROUND

Dr. O'Neill's Invention

The invention at issue concerns treatment of MS, as noted above, a chronic, progressing and debilitating disease. (*See, e.g.*, JTX2000 at 1:15-34; Wynn 473:11-24, 494:7-9; D.I. 376-1 at 10; PDX003-11.) Thought to be an autoimmune disease, MS attacks healthy nerves in the central nervous system. (Wynn 473:25-474:5; Greenberg 107:2-5; PDX003-10.) Specifically, the immune system attacks myelin, the protective sheathing around nerve axons, a portion of the nerve cells. (PDX003-10.) This results in inflammation that causes demyelination, which ultimately leads to axonal loss and death of the nerve cell—the hallmark characteristics of MS. (Wynn 480:11-22, 479:14-21; Greenberg 439:20-440:23; PDX003-10.) The cumulative result of this damage to the nerve cells is scarring, or lesions, in the brain. (Wynn 475:2-476:7.) The damage MS causes to the brain and other areas of the CNS can be imaged using magnetic resonance imaging (“MRI”) techniques. (*Id.*; PDX003-12.) MRI brain scans identify both active inflammation in and long-term damage to brain tissue in MS patients, and these methods are used by doctors to monitor the progress of the disease in patients. (*Id.*) MS can cause severe disability to almost every part or function of the body. (Wynn 474:14-475:1; PDX003-11.)

In 2003, Biogen recognized a need for an oral therapy to treat MS. (JTX2133 at ¶ 10.) At that time, the only FDA-approved treatments were administered by injection. (*Id.*) Dr. O'Neill led Biogen's efforts to address this problem by developing DMF into a much-needed oral medication for MS. (*Id.* at ¶¶ 5, 12; Bozic 365:18-23.)

Dr. O'Neill is a neurologist specializing in neuromuscular diseases. (O'Neill 647:1-18.) He treated MS patients while working at Massachusetts General Hospital before joining Biogen in 2003 as Associate Director, Medical Research. (O'Neill 647:4-9; DTX1104.3 at ¶ 2.) Shortly

after joining Biogen, he participated in a confidential due diligence of the company Fumapharm AG, which was studying fumarates and with whom Biogen was considering entering a licensing transaction. (O'Neill 564:10-19, 589:4-14; JTX2133 at ¶¶ 10-11.)

During his participation in the due diligence in 2003, Dr. O'Neill had an insight into an effective dose of DMF for treating MS. Dr. O'Neill reviewed confidential data Fumapharm generated through, e.g., its studies of Fumaderm[®] (a mixture of fumarates, one of which is DMF) that Fumapharm marketed for treating psoriasis. (O'Neill 564:24-565:2, 589:5-590:6; JTX2133 at ¶¶ 10-11.) These confidential data included safety data for Fumaderm[®] and data generated in Fumapharm's studies relating to a DMF-only drug product for psoriasis. (O'Neill 589:5-590:17; JTX2133 at ¶ 10.) Dr. O'Neill studied these data and "spent a lot of time thinking about the underlying pharmacology of the medicine." (O'Neill 590:13-14; *see also id.* 591:18-22.) In doing so, Dr. O'Neill had an insight that the peak level of the medication in the bloodstream, the " C_{max} of DMF," was what could be driving the efficacy of DMF. (O'Neill 590:24-591:15.) As Dr. O'Neill testified, he believed that efficacy "might be driven by the maximal exposure of the medicine in the circulation as opposed to a continuous exposure of the medicine." (O'Neill 591:4-6.) This insight led Dr. O'Neill to conclude that a daily dose of 480 mg of DMF could achieve the correct "maximal exposure" and be efficacious in treating MS. (O'Neill 590:21-591:2 ("So I believed that 480 milligrams in two divided doses of 240 milligrams of DMF could be efficacious in the treatment of MS . . . I believed it because of the pharmacology of the medicine.")) Dr. O'Neill's identification of this dose would ultimately lead to the development of Biogen's oral treatment for MS: Tecfidera[®].

Biogen's Clinical Development of Tecfidera®

Biogen licensed certain of Fumapharm's rights in DMF and appointed Dr. O'Neill as the Medical Director for Biogen's BG-12 Development Program, which was focused on the development of Tecfidera®. (JTX2133 ¶¶ 11-12.) BG-12 was Biogen's internal and external name for Tecfidera® prior to FDA approval. (JTX2133 at ¶ 11; O'Neill 588:14-21.) As Medical Director, Dr. O'Neill was responsible for designing and leading the clinical development of DMF for MS. (JTX2133 ¶¶ 5, 12, 14, 18; Bozic 365:18-23.) In this role, he communicated with the other members of the BG-12 development program his conception of using 480 mg/day of DMF to treat MS, and proposed testing 480 mg/day DMF in his most preferred design proposals for Biogen's Phase II study of DMF, Biogen's first study of DMF in MS patients. (JTX2035 at 14; Lansden 662:1-663:8, 661:11-14; Bozic 357:19-358:4; JTX2133 at ¶ 19; JTX2013 at ¶¶ 23-24 (the 480 mg DMF per day of BG-12 "was included in Dr. O'Neill's top two designs, and I recall his belief that the 240 mg BID dose would be effective to treat MS patients and should be tested in a clinical trial."); JTX2146.)

On February 19, 2004, Dr. O'Neill presented slides to Biogen's Clinical Trial Review Board ("CTRB") describing four different proposals for the doses to be tested in Biogen's Phase II study. (O'Neill 606:17-607:2; JTX2035 at 14; JTX2133 at ¶ 19.) The CTRB, which included medical, regulatory and commercial team members, was responsible for reviewing and approving clinical study designs, including that of Biogen's Phase II study. (O'Neill 601:12-24; Bozic 355:20-356:13; 368:29-369:4; JTX2133 at ¶ 19; JTX2013 at ¶¶ 23-24; JTX2039.) Dr. O'Neill's first two dosing proposals in his presentation included 480 mg/day dosing arms, reflecting his desire to test his idea of using 480 mg/day DMF to treat MS:

Summary of Dosing options.					
Option	Dosing Regimes				
#1	240 mg/day 2 div dose	360 mg/day 3 div dose	480 mg/day 2 div dose	720 mg/day 3 div dose	
#2	120 mg/day Single dose	360 mg/day 3 div dose	480 mg/day 2 div dose	720 mg/day 3 div dose	
#3	120 mg/day Single dose	360 mg/day 3 div dose		720 mg/day 3 div dose	
#4				720 mg/day 3 div dose	1080 mg/day 3 div dose

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(JTX2035 at 14; *see also* O'Neill 606:17-607:24; Bozic 358:14-359:2; JTX2013 at ¶ 24.) The 480 mg/day dose was Dr. O'Neill's preferred dose. He "was an advocate for 480 milligrams . . . a day of DMF." (O'Neill 565:22-566:1, 605:15-16; *see also* Bozic 366:4-5; Lansden 658:14-20, 662:17-663:8.)

Dr. Carmen Bozic was the Chairperson of the CTRB and had the final authority to approve clinical study protocols. (Bozic 355:19-24; Pretrial Order, D.I. 315 Ex. 1 at ¶ 11.) Dr. Bozic explained that, in its review of Dr. O'Neill's dosing proposals, the CTRB "listened to many different voices on the board in order to make a decision." (Bozic 356:3-5.) Option 1 was Dr. O'Neill's preferred study design and included a 480 mg/day DMF arm and 720 mg/day DMF arm. (JTX2035 at 14; *see also* O'Neill 606:17-607:24; Bozic 358:14-359:2.) Commercial representatives expressed a preference for Dr. O'Neill's option 2, which was Dr. O'Neill's second choice, and which also included a 480 mg/day arm and a 720 mg/day arm. (Bozic 360:8-18, 359:16-22; Lansden 664:19-22; JTX2035 at 20; JTX2133 at ¶ 20.) In the end, although attendees at the meeting reacted positively to Dr. O'Neill's proposal to test 480 mg/day, the CTRB chose

option 3 instead because the CTRB considered it to be a more conventional dose-ranging study. (JTX2039 at 2; *see, e.g.*, Bozic 362:20-363:6, 363:19-364:5, 369:21-24; JTX2036; JTX2133 at ¶ 20.) Option 3 did not provide for the testing in Phase II of Dr. O'Neill's preferred dose of 480 mg/day, but the doses to be tested did bracket that dose such that Biogen could test that dose later in Biogen's Phase III studies. (O'Neill 607:22-608:8, 609:21-610:4, 624:17-22 ("I did accept that we could go forward with [the Phase II MS] study without 240 BID, largely because I knew that we were bracketing that dose and would be able to revisit it once we had chief proof of concept, as we did in the Phase 3 studies."); Bozic 386:19-387:18, 376:12-23, 368:10-14; Lansden 658:11-15; Dawson 684:2-9, 685:19-686:18.) In other words, as Dr. Bozic explained, "[t]he important thing is to establish a dose range where you have safety and where you may have efficacy, and that gives you flexibility to continue to evaluate additional doses further on in Phase 3" (Bozic 367:21-24; *see also* JTX2133 at ¶ 21 ("the 480 mg per day dose could be included in subsequent, pivotal Phase III clinical trials involving patients once Biogen had the benefit of assessing the results (e.g., safety, tolerability, and efficacy data) of the surrounding doses. . .").)

The evidence clearly established that during the Phase II trial and through the planning of Phase III trials, Dr. O'Neill advocated for testing of his preferred 480 mg/day dose. (JTX2039 at 2; JTX2146; Lansden 669:20-670:2, 662:17-663:8, 658:2-10; JTX2193 at 1; O'Neill 605:12-16, 611:11-15, 628:12-19 ("we carried the torch for BID [480 mg/day] right through to our design planning for Phase 3 [and] . . . always remained looking at BID dosing, which is why we included it in the Phase 3 design."), 631:7-12; Bozic 376:12-14.) One of the witnesses was Ms. Cara Lansden, a Manager of Clinical Development, and a key member of the BG-12 team from late 2003 to July 2006. She reported to, and worked closely with, Dr. O'Neill. (Lansden 663:4-5.) According to Ms. Lansden, during the course of the Phase II study, "[Dr. O'Neill] did talk about

[the 480 mg/dose] a lot,” including in “one-on-one meetings” and “hallway conversations” such that “[i]t definitely stood out”—“once the 480-mg dose was not chosen for Phase [II], I basically heard about it for the rest of the year.” (Lansden 658:14-20, 663:4-8, 677:11-13.) According to Dr. Bozic, Chair of the CTRB, Dr. O’Neill “believed that 240 milligrams BID [480 mg/day] should be evaluated in the [Phase II] study. That was very important to him.” (Bozic 366:4-5.) She further testified that while planning for the Phase III trials she “recall[ed] speaking to Gilmore O’Neill at that time, and he thought it was very important to include the 240-milligram BID dose into the Phase 3s.” (*Id.* at 376:4-6.) Dr. Katherine Dawson, who took over as Medical Director of Biogen’s BG-12 program from Dr. O’Neill, testified that “Dr. O’Neill had the idea of using 480 milligrams of DMF to treat MS” and “had wanted to try 480 ever since [she] got to Biogen, which was in March of 2004.” (Dawson 685:7-8, 686:24-25; *see also id.* 682:21-683:7.)

Biogen carried out its Phase II study between 2004 and 2006, testing DMF doses of 120 mg/day, 360 mg/day and 720 mg/day. (JTX2153B at 8, 12.) The 720 mg/day dose demonstrated efficacy in treating MS, while the lower 120 mg/day and 360 mg/day doses did not show any statistically significant effect compared to placebo. (*Id.*) Following this successful proof of concept showing efficacy and safety at the 720 mg/day dose, Biogen moved forward with its plans for its Phase III study. (Dawson 689:11-690:15, 694:11-16; O’Neill 626:1-6; Lansden 653:18-654:19, 671:21-672:9, 678:3-7; JTX2141; JTX2142; JTX2091; JTX2100; JTX2101; Bozic 374:1-377:5; JTX2133 at ¶¶ 36-37; JTX2013 at ¶¶ 94, 98.) This included meetings during the summer of 2006 involving various BG-12 team members including Dr. O’Neill, during which the team discussed, among other things, plans to test Dr. O’Neill’s preferred dose of 480 mg/day. (*See* JTX2142.)

In July 2006, Dr. O'Neill transitioned out of his role as Medical Director of the BG-12 program to oversee other projects at Biogen. (O'Neill 554:12-18, 612:8-14.) Dr. Dawson took over for Dr. O'Neill, becoming the new Medical Director of the BG-12 program. (Dawson 690:21-691:17; JTX2091 at 1; JTX2133 at ¶ 38.) During this transition, the BG-12 team was preparing for Biogen's Phase III studies, which the BG-12 team believed would include testing of Dr. O'Neill's preferred 480 mg/day dose. (Dawson 683:1-7.) An important aspect of Phase III planning was a meeting with the FDA known as an End of Phase II ("EOP2") meeting. (JTX2133 at ¶ 37.) During this meeting, which took place on August 30, 2006, Biogen sought the FDA's approval for its Phase III study design, including the Phase III proposed endpoints, patient population, maximum acceptable dose and other issues. (*Id.*; Bozic 378:17-21.) Dr. Dawson and the team prepared for the EOP2 meeting, and the team and she remained in communication with Dr. O'Neill leading up to and following the meeting, though Dr. O'Neill did not participate in that meeting. (JTX2133 at ¶ 38; Dawson 687:14-22, 698:8-13, 705:3-11; JTX2102.)

Contrary to Mylan's suggestion that Biogen's plans regarding which doses to test "took a significant turn" after its August 30, 2006 EOP2 meeting with the FDA (Mylan Br. at 6), Biogen had begun preparations to test the 480 mg/day dose *prior to* the EOP2 meeting. (JTX2142 at 2; JTX2091 at 2; Dawson 689:11-690:15, 691:18-692:12; JTX2100 at 2; Bozic 374:1-20; Lansden 671:21-672:9, 653:24-654:19; JTX2133 at ¶ 37; JTX2013 at ¶¶ 94, 98.) In fact, by July 5, 2006, Biogen had calculated the number of patients needed to test 480 mg/day, as well as 720 mg/day, in its Phase III trials. (JTX2091 at 2; *see also* Lansden: 673:21-675:17.) Biogen focused its submissions to the FDA for the EOP2 meeting, however, on the 720 mg/day dose because Biogen only needed FDA agreement as to the highest dose to be tested, which was 720 mg/day. (JTX2133 at ¶ 37; JTX2103 at 22, 63-91; Dawson 699:1-700:13, 695:14-17, 704:9-22; O'Neill 635:3-5;

JTX2142 at 2 (“It is not necessary to have the 480 mg version of the protocol in the briefing document.”); Bozic 386:1-18, 378:17-379:21.) As Dr. Dawson explained, “[f]or the end of Phase 2 meeting, all we need to get agreement with the FDA is what the highest dose is [T]he lower doses are at our discretion.” (Dawson 699:4-7; *see also* Bozic 380:24-382:4.) Moreover, Biogen needed to focus its discussion in the EOP2 meeting because of the limited time Biogen had in this meeting with the FDA, which only lasted for 90 minutes, and the need to spend time discussing other critical elements including the use of the reference comparator. (Bozic 379:13-21; Dawson 701:9-13, 694:11-21; O’Neill 633:5-17; PTX108 at 5, 8.)

On the morning of the EOP2 meeting, Biogen received written FDA feedback on numerous issues, including dosing. (PTX108 at 7-8; *see, e.g.*, Dawson 684:24-685:4, 702:9-703:11.) The FDA suggested Biogen consider including lower doses in its Phase III studies, including, “e.g., 240 BID [480 mg/day] or 120 TID [360 mg/day]” to “improve patient compliance and/or minimize dropouts.” (PTX108 at 7-8.) The FDA’s comments thus related to safety concerns and even suggested that Biogen consider including in its Phase III study the 360 mg/day dose that was ineffective in Phase II. (PTX108 at 7-8; JTX2104 at 1.)

Biogen commenced its first of two Phase III trials on March 14, 2007 (the DEFINE trial), and its second (the CONFIRM trial) on July 28, 2007. Both trials tested Dr. O’Neill’s preferred 480 mg/day dose. (JTX2133 at ¶ 40; JTX2110 at 28, 38; JTX2108 at 12, 23; Dawson 709:22-25, 704:2-8, 708:12-16.)

Biogen’s Submission of the ’514 Patent Application

Following the completion in 2006 of the Phase II trial showing the efficacy of 720 mg/day of DMF and shortly before the commencement, in March 2007, of the Phase III DEFINE clinical trial testing of Dr. O’Neill’s preferred 480 mg/day dose and the 720 mg/day dose, Biogen filed, on

February 8, 2007, the provisional application that led to the '514 patent and included in the provisional application the specific disclosure of using “from about 480 mg to about 720 mg per day” DMF to treat MS. (JTX2182 at 2, 36.) Consistent with the Phase III design, Biogen disclosed those two doses as the narrowest, most preferred range of doses to be used. (*Id.* at 36.)

Biogen’s patent application also included work by Dr. Matvey Lukashev, a research scientist at Biogen who had joined the BG-12 team in 2005. (Lukashev 272:17-22, 276:12-17.) Dr. Lukashev’s background was in molecular and cellular biology and he was responsible for mechanism of action and pre-clinical work on BG-12. (Lukashev 270:18-24; 273:15-22, 277:11-24.) He had no clinical experience and was not responsible for the clinical aspects of the team’s work. (Mylan Br. at 9 (“Dr. Matvey Lukashev, a laboratory researcher who had no clinical experience or responsibilities”); Dawson 685:5-12.) Dr. Lukashev’s inventions contributed to claims 17-19 of the '514 patent, which involve the expression level of NQO1 after DMF administration and are not asserted in this litigation. (Lukashev 313:2-12, 315:19-316:15.) Dr. Lukashev’s contributions also included various compound screening methods that are also described, but not claimed, in the '514 patent.

Biogen’s Phase III Results

As discussed above, Biogen conducted two pivotal placebo-controlled, double-blind Phase III clinical trials for BG-12 in MS, DEFINE and CONFIRM. (JTX2173 at 847; JTX2133 at ¶ 40.) Over 1200 patients in 28 different countries were randomly assigned in the DEFINE trial to one of three treatment groups: (1) 240 mg DMF BID (480 mg/day), (2) 240 mg DMF TID (720 mg/day), and (3) placebo. (JTX2088 at ¶ 11.) Over 1400 subjects in 28 different countries participated in Biogen’s CONFIRM trial, which also included dosing of DMF at 480 and 720 mg/day. (JTX2133 at ¶¶ 40-41.)

These Phase III trials showed an unexpected magnitude of efficacy where the 480 mg/day dose “met all primary and secondary endpoints” including both MRI and clinical endpoints, e.g., reduction in annual relapse rate, and did so “with a *high level of statistical significance*.” (JTX2088 at ¶¶ 11-12, 15) (emphasis in original).) Moreover, the results for the 480 mg daily dose were similar to those with the 720 mg/day dose for each end point measured. (*Id.*) According to Dr. O’Neill: “I was very pleased to see that 480 milligrams demonstrated not only efficacy at a significant level but at the level that it showed it [t]hat it actually showed a marked and statistically significant reduction in the annualized relapse rate [a]nd other efficacy outcomes.” (O’Neill 598:3-10.)

Biogen’s Prosecution of its ’514 Patent

In June 2011, Biogen amended the claims to recite a method of treating MS with 480 mg/day DMF and/or MMF and the title to reflect the invention now claimed, and specifically identified to the Patent Office exemplary portions of the patent specification providing support for the amended claims. (DTX1656.1-5, 11.) In October 2011, Biogen also amended the inventorship to add Dr. O’Neill, who conceived of the claimed treatment methods. (DTX1019.13-15.) Biogen did not make any changes to the patent specification. (DTX1656.1-5, 11.)

In October 2011, Biogen also submitted Dr. Dawson’s declaration detailing the results of the first of Biogen’s Phase III studies and describing how they were unexpected in light of Biogen’s Phase II study. (JTX2088; D.I. 376 at 15.) For example, pointing to results seen on MRI brain scans and in additional measures, including reductions in annualized relapse rates, Dr. Dawson explained that the “positive and clinically meaningful results obtained with the 480 mg per day dose of DMF were unexpected,” and “[e]ven more unexpected . . . was the magnitude of the treatment effect of the [first Phase III] study—the 480 mg/day dose demonstrated similar efficacy

to the 720 mg/day dose on both clinical and MRI measures of MS disease activity—with a *high level of statistical significance*.” (JTX2088 at ¶¶ 14-15 (emphasis in original).)

The Patent Examiner never issued any rejections relating to an alleged lack of written description support for the claimed treatment methods. The Examiner did question however, in the context of an obviousness rejection, whether the “particular combination” recited in the claimed method was “described in the specification as filed.” (JTX2173 at 388, 890-896.) Biogen responded by noting that the specification focuses on treating MS with DMF and describes the use of 480 mg/day DMF, pointing to many of the same portions of the patent specification that Dr. Wynn identified in his trial testimony as further discussed below. (JTX2173 at 911-14.) Biogen explained to the Examiner that the “specification contains ample teachings directing a person of ordinary skill in the art to the claimed invention (treating MS with DMF/MMF using a 480 mg/day dose).” (JTX2173 at 911-12.) For example, the “specification focuses on treating MS with DMF and/or MMF” and provides “a number of blaze marks . . . clearly direct[ing] a person of ordinary skill in the art to use DMF and/or MMF in treating MS.” (JTX2173 at 912-13.) The specification also “teaches the claimed dose of 480 mg/day DMF and/or MMF” by “disclos[ing] a limited number of progressively narrowing effective dose ranges of DMF or MMF and disclos[ing] the 480 to 720 mg/day dosage range as the narrowest range for the treatment of a patient with a neurodegenerative disease.” (JTX2173 at 913-14 (underline in original).) The Examiner subsequently allowed the claims. (JTX2173 at 951.)

Following the completion of Biogen’s Phase III study, Biogen filed in May 2011 another patent application, 14/119,373 (“the ’373 Application”), directed to aspects of Biogen’s Phase III trial data. (DTX1169.) Biogen’s Phase III studies were large and generated data relating to multiple endpoints. (JTX2088 at ¶ 11.) The claims of Biogen’s ’373 application focused on these

new and specific discoveries relating to, for example, the “reduced frequency of relapse,” the “reduced probability of relapse,” the “reduced annualized relapse rate,” and “the reduced risk of disability progression.” (*See, e.g.*, DTX1169 at Claims 1, 5, 8, 11, 14, 39 and 40.) Mylan’s speculation as to why Biogen filed the ’373 Application, Mylan’s allegation that Biogen “faced a major problem” with the application, and Mylan’s speculation as to why Biogen abandoned this application are entirely unsupported by the evidence and Mylan does not offer any citations to the evidence. These unsupported speculations about a different application are also irrelevant to the sole issue in this case—the written description of the ’514 patent.

Biogen did not, as Mylan asserts, “repurpose” the ’514 patent application. Biogen added new patent claims to the ’514 patent application, as is permitted and often happens during patent prosecution, but the specification remained the same through the course of prosecution before the PTO. Finally, Mylan’s speculations about Biogen’s prosecution of the ’514 patent are in direct conflict with the record. When Biogen first introduced its method of treatment claims during prosecution, it informed the PTO where those methods of treatment are described in the patent specification. (JTX2173 at 64-67.) Biogen also updated the inventorship to include Dr. O’Neill to account for the new method of treatment claims, in accordance with the law. (DTX1019.13-15.) Biogen further informed the PTO about prior art relating to DMF as well as Biogen’s later Phase III study results. (*See, e.g.*, JTX2173 at 134, 146-49; JTX2088 at ¶¶ 11-16.) Having considered this evidence, the PTO found Biogen’s patent claims patentable and issued the ’514 patent, and in doing so never made any rejection for lack of written description support. (JTX2173 at 951.)

III. THE '514 PATENT SATISFIES THE WRITTEN DESCRIPTION REQUIREMENT

The trial record confirms that the '514 patent specification describes the claimed invention and that Mylan has not met its burden of proving that the claimed invention lacks written description support.

A. Mylan Bears the Burden of Proving that Biogen's Presumptively Valid Patent Does Not Satisfy the Written Description Requirement

Mylan bears the burden of proving its invalidity defense by clear and convincing evidence. 35 U.S.C. § 282; *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 97 (2011); *Mas-Hamilton Grp. v. LaGard, Inc.*, 156 F.3d 1206, 1216 (Fed. Cir. 1998) (“[T]he presumption of validity remains intact and the ultimate burden of proving invalidity remains with the challenger throughout the litigation.”); *see also Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1534 (Fed. Cir. 1983) (“In the end, the question is whether all the evidence establishes that the validity challenger so carried his burden as to have persuaded the decisionmaker that the patent can no longer be accepted as valid.”); *Dey L.P. v. Teva Parenteral Meds., Inc.*, 6 F. Supp. 3d 651, 663 (N.D. W. Va. 2014) (same).

Mylan's heavy burden comes with the added burden in this case that the Patent Office raised, in the context of an obviousness rejection, the issue of written description support during prosecution of the '514 patent.² The Federal Circuit has recognized the added burden a patent challenger faces in “overcoming the deference that is due to a qualified government agency

² As discussed above, the Examiner questioned whether the “particular combination” recited in the claimed method was “described in the specification as filed.” (JTX2173 at 388, 890-96.) (See MPEP Rev. 8th ed. at 1302.01 (explaining that before a patent issues, examiners should conduct a final review “to make certain” that “all formal and substantive (i.e., statutory) requirements” are met “and that the language of the claims is enabled by, and finds adequate descriptive support in, the application disclosure as originally filed.”); *see also id.* at 2163 (providing guidelines for the examination of the written description requirement that “are intended to form part of the normal examination process”).

presumed to have properly done its job, which includes one or more examiners who are assumed to have some expertise in interpreting the references and to be familiar from their work with the level of skill in the art and whose duty it is to issue only valid patents.” *Shire, LLC v. Amneal Pharm., LLC*, 802 F.3d 1301, 1307 (Fed. Cir. 2015) (quoting *PowerOasis, Inc. v. T-Mobile USA Inc.*, 522 F.3d 1299, 1304 (Fed. Cir. 2008)).

“The written description requirement [of Section 112]³ is met when the disclosure ‘allows one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.’” *Allergan*, 796 F.3d at 1308 (quoting *Enzo*, 323 F.3d at 968). Written description “is about whether the skilled reader of the patent disclosure can recognize that what was claimed corresponds to what was described; it is not about whether the patentee has proven to the skilled reader that the invention works, or how to make it work.” *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1191 (Fed. Cir. 2014). Indeed, there is no requirement that the patent specification must contain “either examples or an actual reduction to practice.” *Ariad*, 598 F.3d at 1352. Rather, “the test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art,” *Ariad*, 598 F.3d at 1351, to determine whether “the patentee has provided an adequate description that ‘in a definite way identifies the claimed invention’ in

³ Paragraph 1 of 35 U.S.C. § 112 was replaced with Section 112(a) by the America Invents Act (“AIA”), Pub. L. No. 112-29, § 4(c), 125 Stat. 284, 296 (2011). Because the ’514 patent claims priority to February 8, 2007, pre-AIA Section 112 applies to the asserted claims. *See* Pub. L. No. 112-29, § 4(e), 125 Stat. 284, 297 (making the AIA changes to Section 112 applicable to “any patent application that is filed on or after” September 16, 2012). Paragraph 1 of pre-AIA 35 U.S.C. § 112 provides the written description requirement as well as the enablement and best mode requirements (Mylan does not challenge either enablement or best mode): “The specification shall contain a written description of the invention [i.e., the written description requirement], and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same [i.e., the enablement requirement], and shall set forth the best mode contemplated by the inventor of carrying out his invention [i.e., the best mode requirement].”

sufficient detail such that a person of ordinary skill would understand that the inventor had made the invention at the time of filing.” *Allergan*, 796 F.3d at 1308 (quoting *Ariad*, 598 F.3d at 1352).

Moreover, “claimed subject matter need not be described in haec verba in the specification in order for that specification to satisfy the description requirement” *In re Smith*, 481 F.2d 910, 914 (C.C.P.A. 1973); *see also Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Rather, “the requirement is met if a [POSA] would find it is ‘reasonably clear what the invention is and that the patent specification conveys that meaning.’” *Pfizer Inc. v. Teva Pharms. U.S.A., Inc.*, 882 F. Supp. 2d 643, 699-700 (D. Del. 2012) (quoting *All Dental Prodx, L.L.C. v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779 (Fed. Cir. 2002)).

Mylan points to evidence relating to the distinct legal concept of obviousness in its written description arguments. Written description and obviousness, however, are separate inquiries based on distinct analyses of different types of evidence. *Compare* 35 U.S.C. § 112 (“The **specification** shall contain a written description of the invention”) (emphasis added) *with* 35 U.S.C. § 103 (“[T]he differences between the subject matter sought to be patented and the **prior art**”) (emphasis added). Obviousness determinations, including whether the invention demonstrates unexpected properties compared to the prior art, are not based on a patent specification’s disclosure but rather are assessed based on the knowledge that a skilled artisan would have *before* reading the patent. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Written description, however, is based on the specification’s disclosure, i.e., with the patent in hand, and how it would be understood by a skilled artisan. *See Ariad*, 598 F.3d at 1351 (“[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.”).

As set forth below, the ’514 patent specification meets the written description requirement.

B. The Specification Demonstrates Possession of the Claimed Invention

The parties agree that the definition of a person of ordinary skill in the art (“POSA”) with respect to the ’514 patent claims is a person having at least a medical degree with at least three years of training in neurology and at least three years of clinical experience in treating MS. (*See* Greenberg 113:18-25; Wynn 470:10-16.) As described in detail below, Dr. Wynn, a skilled artisan in the field of the claimed invention, testified at trial how the specification describes all aspects of the claimed invention to a skilled artisan like himself. (Wynn 494:1-18, 470:24-471:5, 478:7-19.) As discussed below, the ’514 patent provides broad and detailed disclosure of Biogen’s research and development activities relating to multiple sclerosis, which the specification categorizes according to five specific methods. Especially relevant here is Method 4, which relates to a method of treating neurological diseases such as MS with compounds like DMF and MMF. (JTX2000 at 8:34-53, 3:1-4, 3:13-14.) The ’514 patent links through Method 4 each of the three recited elements of the asserted claims: (1) a method of treating MS with (2) DMF and/or MMF (3) at a dose of 480 mg per day. (Wynn 494:1-18, 470:24-471:5, 478:7-19; PDX003-24; JTX2000 at 27:58-30:28; Greenberg 397:19-398:1.)

1. The Specification Describes Treatment of MS

The ’514 patent focuses on multiple sclerosis, describing “from beginning to end . . . the treatment of multiple sclerosis.” (Wynn 484:12-19, 479:2-480:22, 494:4-9; *see, e.g.*, JTX2000 at Abstract, Title, 1:12-14; 1:15-52, 3:10-14, 20:63-22:18.) The specification begins by discussing in detail the characteristics, prevalence and goals for treatment of MS. (JTX2000 at 1:15-52; PDX003-14.) Its first substantive paragraph highlights MS as the neurological disease for treatment. (*See, e.g.*, JTX2000 at 1:12-52.) The specification next explains that MS is “characterized by inflammation in parts of the CNS, leading to the loss of the myelin sheathing around neuronal axons (demyelination), loss of axons, and the eventual death of neurons,

oligodendrocytes and glial cells,” which the parties’ experts agreed are the characteristics or “hallmarks” of MS. (JTX2000 at 1:15-20; Greenberg 414:9-10; Wynn 440:3-23, 479:2-480:22; PDX003-14.) The specification then discusses the prevalence of MS, the “most common cause of nontraumatic disability in young individuals” (Wynn 473:22-24), and goals for treatment as of 2007, namely “reduc[ing] inflammation,” “[p]romoting CNS remyelination as a repair mechanism and otherwise preventing axonal loss and neuronal death.” (JTX2000 at 1:35-52; Wynn 479:5-21; PDX003-14; Greenberg 400:10-21, 402:9-14.)

The specification then provides an overview of the broad disclosure in the specification, categorized according to five methods. Methods 1-3 are directed to methods of screening for compounds to treat neurological diseases. (JTX2000 at 6:18-8:33.) Methods 4 and 5 are directed to methods for treating neurological diseases including MS. (JTX2000 at 8:34-9:15; Greenberg 404:2-3.) Method 4 is directed to the use of a compound such as DMF, while Method 5 relates to the use of such a compound in combination therapy along with other compounds having different activity. (JTX2000 at 3:1-4, 3:5-9, 3:13-14, 8:34-53.) Method 4 thus directly pertains to the claimed methods of treating MS with DMF and/or MMF. (JTX2000 at 8:34-53, 3:1-4, 3:13-14.) The specification includes additional descriptions of treatment Method 4 at column 4, lines 33-38, and column 8, lines 24-28, lines 35-53. These additional descriptions indicate that treatment Method 4 can be used to “slow or prevent demyelination, axonal loss and/or neuronal death,” the same “hallmarks” of MS described at column 1, lines 15-20 of the ’514 patent. (Wynn 479:2-480:22.) These discussions of Method 4 repeatedly emphasize that MS is the neurological disease targeted for treatment by this method and is a focus of the patent. Indeed, “multiple sclerosis . . . is listed . . . over 30 times throughout the specification[.]” (Wynn 518:19-22; *see* Wynn 510:12-

13; 518:25-519:1; JTX2000 at Title, Abstract, 1:12-52, 2:9-22, 3:13-14, 5:6-8, 5:15-24, 7:13-32, 16:21-26, 16:42-59, 16:66-17:58.)

An example in the '514 patent also demonstrates that the specification and the disclosed methods focus on MS. Example 3 employs an animal model for MS, the Experimental Autoimmune Encephalomyelitis (EAE) mouse model, which is also explained in detail at column 16, line 67 to column 17, line 38 of the specification. (JTX2000 at 20:60-22:13.) As Biogen's Dr. Wynn explained at trial, skilled artisans would have understood by 2007 that the EAE model, used solely for MS, was the "most common model . . . use[d] for studying compounds for treating multiple sclerosis." (Wynn 483:17-19, 484:5-9, 484:16-17, 509:8-10, 512:15-17; *see* Greenberg 413:23-414:10.)⁴

2. The Specification Describes Treating MS with DMF and/or MMF

The specification links treating MS with DMF and/or MMF through treatment Method 4. The description of Method 4 in the specification repeatedly highlights DMF and MMF as examples of compounds for use in this method for treating neurological diseases like MS. (*See* JTX2000 at 3:1-4, 4:29-32, 8:24-28, 8:34-53, 11:47-50; PDX003-15, 16, 17.) This disclosure of treating neurological diseases like MS with DMF and/or MMF is detailed in each description of Method 4, appearing at column 3, lines 1-4, column 4, lines 29-32 and column 8, lines 35-38 ("In some embodiments method 4 comprises administering to the mammal a therapeutically effective amount of at least one neuroprotective compound having Formula I, II, III, or IV, e.g., a fumaric acid

⁴ Mylan argues in a footnote that "[e]xample 3 was absent from Biogen's specification as filed in 2007, so Biogen cannot rely on it now to satisfy the written description requirement as of the 2007 filing date." (Mylan Br. at 17 n.6.) However, the provisional application as filed identified and described the EAE model as an animal model for MS (JTX2182 at 32-34), thus teaching a skilled artisan in 2007 that the specification is focused on treating MS. Mylan does not, of course, dispute that Example 3 is in the specification that Biogen filed with the Patent Office on February 7, 2008, and contained in the '514 patent.

derivative (e.g., DMF or MMF).” (JTX2000 at 4:29-32.) Mylan acknowledges that the disclosed treatment Methods 4-5 use DMF and that the specification “identifies DMF” for use in those methods. (Mylan Br. at 17.) Dr. Greenberg testified that “in Method 4 on Column 8, it discusses methods of treating a neurologic disease by administering to the subject at least one compound that is at least partially structurally similar to DMF or MMF.” (Greenberg 407:3-6.) Dr. Wynn explained, and Mylan does not dispute, that “partially structurally similar includes DMF and MMF, which are obviously more than partially structurally similar but are identical to DMF and MMF.” (Wynn 485:15-17; *see also id.* 485:3-8, 485:23-486:2 (“[I]n [column 8] line 38, again, it states ‘[at least] partially structurally similar to DMF or MMF.’ Skipping down to line 44, it states ‘a fumaric acid derivative, e.g., DMF or MMF,’ clearly teaching me that DMF and MMF are compounds that being taught.”) (Wynn 494:14-18; Greenberg 434:14-435:11; 405:17-406:1; *see also* Mylan Br. at 5.) The examples similarly disclose experiments using only DMF and/or MMF, further indicating that the specification, including its disclosed treatment methods, are focused on these specific compounds. (JTX2000 at 19:62-22:14; *e.g.*, JTX2000 at 22:12-13 (“The results [from Example 3], shown in Figs. 3 and 4, demonstrate MMF and DMF activation of Nrf2 in vivo.”).)

3. The Specification Describes 480 mg/day DMF As An Effective Dose To Treat MS

The ’514 patent specification states that “[i]n some embodiments method 4 comprises administering to the mammal a therapeutically effective amount of at least one neuroprotective compound having Formula I, II, III, or IV, e.g., a fumaric acid derivative (e.g., DMF or MMF).” (JTX2000 at 4:29-32.) The specification defines “therapeutically effective dose” and “therapeutically effective amount” broadly, tying this definition of these terms to the treatment of MS by using the same language the patent repeatedly uses to characterize MS, i.e., the “hallmarks”

of MS, “demyelination, axonal loss, and neuronal death.” (JTX2000 at 5:52-59, 4:29-32, 8:39-44; Wynn 531:21-532:21, 494:4-9.) As to specific amounts of DMF to be used, the specification states:

For example, an *effective dose of DMF* or MM[F] to be administered to a subject *orally* can be from about 0.1 g to 1 g per [d]ay, 200 mg to about 800 mg per day (e.g., from about 240 mg to about 720 mg per day; or from *about 480 mg to about 720 mg per day*; or about 720 mg per day).

(JTX2000 at 18:58-62 (emphasis added).) The specification thus identifies 480 mg/day of DMF as the lowest dose in the narrowest, most preferred range (480-720 mg/day) of effective doses for oral administration. (Wynn 532:25-533:6, 489:9-491:15; PDX003-17; *see* Greenberg 439:12-16.) This narrowest range specifically links the claimed dose of 480 mg/day to 720 mg/day of DMF, and Mylan and both experts agreed that a POSA would have known by February 8, 2007 from the results of Biogen’s Phase II trial that 720 mg/day of DMF was an effective dose for treating MS. (Wynn 490:19-491:1, 476:12-17, 519:16-18, 532:25-533:6; Greenberg 428:3-6.) Biogen’s expert Dr. Wynn testified that the paragraph above “calling one to 480 to 720, 720 being the known effective dose, 480 to 720 being the most narrow range listed in the patent specification, hence drawing me to that specifically, the 480 dose.” (Wynn 490:22-491:1; *see also id.* 529:24-530:1, 519:16-18.) Mylan’s Dr. Greenberg agreed that this disclosure teaches “narrower and narrower” dose ranges. (Greenberg 423:24-25.)

This paragraph concludes by describing that 720 mg/day, “[f]or example,” may be administered in separate “equal doses.” (JTX2000 at 18:63-64.) The dosing paragraph does not limit such separate administration to 720 mg/day, but teaches that such separate administration applies to the other effective DMF doses, such as 480 mg/day. (*Id.*)

Mylan argues that “[f]or DMF or MMF, the specification states that dosage likewise varies depending on multiple factors” (Mylan Br. at 5; *see also id.* 17; Greenberg 415:18-21; *id.*

419:22-423:21.) The specification, however, provides information accounting for each of the factors with respect to DMF and MMF, explaining how to account for the “route of administration, excipient usage, and the possibility of co-usage with other therapeutic treatments including use of other therapeutic agents.” (JTX2000 at 18:54-58.) The specification describes *orally* administering an “effective dose” of DMF or MMF, thus specifying the route of administration. (*Id.* 18:58-59, 19:26-28, 5:47-59.) In addition, the dosing disclosure at 18:58-62 of the ’514 patent does not discuss co-usage, and thus co-usage is not a factor that needs to be considered for the claimed invention. (*See* JTX2000 at 18:58-62.) As to excipients, the specification points the skilled artisan, for example, to U.S. Patent No. 6,509,376 (“the ’376 patent”) describing “formulations containing DMF and/or MMF,” including the multiparticulate formulation Biogen used in its Phase II study. (JTX2000 at 19:26-27, 22:14-15; Wynn 491:16-493:13.) The patent specification thus provides specific and detailed teachings that are consistent with the specification’s focus on using 480 mg/day to 720 mg/day of DMF.

4. The Specification Describes the Claimed Invention as an Integrated Whole

As Dr. Wynn’s testimony demonstrates, the ’514 patent specification describes to a skilled artisan all elements of Dr. O’Neill’s claimed invention, directed to a “narrow and very specific procedure” (Mylan Br. at 1) of using a specific drug (DMF and/or MMF) to treat a specific disease (MS) with a specific dose (480 mg/day), and links these elements through treatment Method 4. (Wynn 494:17-18, 470:24-471:5, 478:7-19; PDX003-24.) The specification focuses on MS throughout. The detailed disclosure of Method 4 specifically highlights DMF and MMF as examples of compounds to use in treating neurological diseases like MS. The specification further discloses that “some embodiments of method 4 . . . comprise[] administering . . . a therapeutically effective amount of at least one neuroprotective compound . . . e.g., DMF or MMF.” (JTX2000

8:39-44; Wynn 488:4-9.) The specification then guides a skilled artisan to the dose of 480 mg/day to treat this disease by disclosing it as the lowest dose in the narrowest, most preferred dose range, connected to a known effective dose in treating MS. Accordingly, the '514 patent provides written description for Dr. O'Neill's claimed treatment method.

C. Mylan Failed To Meet its Burden of Proof

Mylan presents arguments concerning unsubstantiated facts and assertions that are also unrelated to the written description inquiry and therefore cannot negate the clear showing of written description support for the claimed invention. Mylan further applies an incorrect legal standard, demanding more disclosure than is required. These arguments cannot overcome the '514 patent's written description of the claimed invention.

1. Mylan's "Repurposing" Arguments are Both Factually Inaccurate and Legally Irrelevant to the Written Description Inquiry

Mylan asserts that Biogen "repurposed" the '514 patent specification, transforming it from a patent directed to screening methods to one directed to treatment methods, and therefore the '514 patent lacks written description support for the claims. (*See, e.g.*, Mylan Br. at 7-9.) Mylan is incorrect. As explained above, Biogen amended the claims during prosecution, as is very common. (*See supra*, Section II, "Biogen's Prosecution of its '514 Patent.") The specification, however, disclosing both screening methods and methods of treating neurological diseases, remained unchanged during prosecution.

Mylan's focus on aspects of the disclosed invention that do not relate to the asserted claims is thus irrelevant. Patent applications may properly describe multiple inventions and claim those inventions in turn. *See* 35 U.S.C. § 121; 37 C.F.R. § 1.41(a). That is precisely what Biogen did here. The '514 patent does describe screening methods, corresponding to Methods 1-3 in the specification, that do not relate to the asserted claims, and the specification provides detailed

discussion of the discoveries relating to those methods. But these discussions do not erase the descriptions of the claimed methods of treating MS that correspond to Method 4 as discussed in detail above. Indeed, Mylan's expert Dr. Greenberg agreed that "Method 4 and 5 discuss methods of treating neurological diseases." (Greenberg 404:2-3; *see also id.* 403:12-20; 404:7; 405:15-406:1; 406:6-15; 406:23-407:15.)

Furthermore, Mylan's claims concerning Biogen's alleged motives, in addition to being unsupported by the record, are legally irrelevant. The written description analysis must focus on the disclosure in the specification, not the applicant's alleged intent. *See Ariad*, 598 F.3d at 1351 ("[T]he [written description] test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.").

Mylan's reliance on testimony of Dr. Lukashev (*see* Mylan Br. at 4, 5, 6, 9, 17 and 19) also does not bear on or negate the patent specification's descriptions of the claimed methods of treatment. Dr. Lukashev is not a skilled artisan with respect to the claims at issue and under the POSA definition to which Mylan and Biogen agreed. (Lukashev 270:18-24; 273:15-22, 277:11-24; Dawson 685:5-12; *see* Mylan Br. at 9.) Dr. Lukashev is not a clinician, and his work was directed to "elucidat[ing] the mechanism of action" for BG-12. (Lukashev 273:15-22, 270:18-24, 277:11-24.) Notably, he was "not involved in clinical decision-making" relating to BG-12. (Lukashev at 273:21-22.) Dr. O'Neill and he both worked on the BG-12 program team, with Dr. O'Neill focusing on the clinical development of the product and Dr. Lukashev studying the mechanism of action. (Lukashev 285:19-286:20; JTX2196 at 1; Lansden 655:16-656:2; JTX2133 at ¶¶ 12-13; JTX2013 at ¶ 17; Dawson 685:9-12.) Dr. Lukashev's inventive work related to the screening methods disclosed in the '514 patent and detailed in Methods 1-3, not the methods of treatment in the asserted claims. (Lukashev 313:2-12, 315:19-316:15.) As Mylan acknowledges,

he was “a laboratory researcher who had no clinical experience or responsibilities” (Mylan Br. at 9) and he is thus not a person of ordinary skill in the art with respect to the claims at issue. That Dr. Lukashev was the only initially named inventor does not negate written description support for the claimed invention. Amendments to inventorship are appropriate and required to conform with changes as to what is claimed. 35 U.S.C. § 116(a); 37 C.F.R. § 1.41(a). Biogen therefore properly added Dr. O’Neill as an inventor when amending the claims to focus on his method of treating MS. (DTX1019.13-15.)

2. Mylan Demands More Than Written Description Law Requires

Mylan argues that the ’514 patent “contains no data or examples showing administration, much less effectiveness of 480 mg doses of DMF for treating MS.” (Mylan Br. at 17; *see also id.* at 19.) Here, however, where the specification describes the three elements of the claimed invention—the disease to be treated, the molecule to be used, and the treatment dose—linking them through treatment Method 4, the law does not require data as to efficacy of the claimed method of treatment. The Federal Circuit has repeatedly held that a patent specification need not include “experimental data demonstrating effectiveness,” a “theory or explanation of how or why a claimed composition will be effective,” or an actual “reduc[tion] to practice.” *Nuvo Pharms. (Ireland) Designated Activity Co. v. Dr. Reddy’s Labs, Inc.*, 923 F.3d 1368, 1380 (Fed. Cir. 2019). Moreover, the written description requirement “is not about whether the patentee has proven to the skilled reader that the invention works.” *Alcon*, 745 F.3d at 1191 (citing *Ariad*, 598 F.3d at 1352). Rather the specification must convey with “reasonable clarity” that the inventor was in possession of the claimed invention. *Nuvo*, 923 F.3d at 1376. That is what the ’514 patent specification does.

3. Mylan and Its Expert Ignore The Disclosure of the Claimed Methods And The State of The Art

Dr. Greenberg acknowledged that his analysis did not consider all disclosures relating to the claimed invention. For example, Dr. Greenberg disregarded the '514 patent's definition of "therapeutically effective amount," admitting on cross-examination that he did not consider "therapeutically effective dose" or "therapeutically effective amount" defined in column 5, lines 52-59: "I know for sure . . . we didn't call out this specific paragraph." (Greenberg 440:24-441:9.) As explained above, the patent ties the concept of "therapeutically effective amount" to "demyelination, axonal loss, and neuronal death," which the parties agreed are the "hallmarks" of MS. (Wynn 494:17-18; Greenberg 441:12-22; *see supra*, Section III.B.1.) Mylan's expert thus failed to consider a key disclosure concerning treatment of MS, recited in certain asserted claims, in his trial testimony.

Dr. Greenberg also improperly focused on evidence relating to the issue of the non-obviousness of the claimed invention. In fact, Dr. Greenberg's written description testimony was premised on statements by Biogen in the prosecution history relating to obviousness and not written description. In fact, Dr. Greenberg postured his written description opinion as based Biogen's statements regarding non-obviousness, testifying that "if [he] were to credit Dr. Dawson's [non-obviousness] opinion [in her declaration] as true," or "under the assumption that Dr. Dawson's [non-obviousness] statements" were correct, then nothing "in the patent specification . . . would convey to skilled artisans that the inventors had possession of a method of treating MS using 480 [mg/day] of DMF." (Greenberg 396:20-397:15; 427:5-11.) As discussed above, however, obviousness determinations examine the state of the art *without* the patent's teachings, while written description determinations examine the patent's disclosure. Dr. Dawson's non-obviousness opinions were directed to what the skilled artisan would have believed without

the teachings of the '514 patent in hand, i.e., what would have been expected based on the state of the art *before reading the patent*, not to what the skilled artisan would have thought with that teaching in hand, which is the proper inquiry in a written description analysis. *See Ariad*, 598 F.3d at 1351 (“[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.”).

Dr. Greenberg also incorrectly testified that the disclosure in the specification of progressively narrowing ranges of oral doses of DMF and/or MMF “doesn’t anchor to a therapeutically effective dose for [MS]” (Greenberg 424:5-6) and that “at no point do any of those doses get tied to therapeutic efficacy.” (*Id.* at 425:11-12.) He further stated that “[t]he narrowing of ranges here . . . a skilled artisan wouldn’t read this and have any knowledge that one particular dose relative to being [a] therapeutically effective dose for MS existed as an entity.” (*Id.* at 425:13-16.) This testimony disregards the fact that 480 mg/day is directly linked, through the narrowest disclosed range of doses, to 720 mg/day, a *known effective dose* for treating MS as of February 2007. (*See Wynn* 476:12-17, 490:22-491:1, 491:8-15, 495:10-20; PDX003-17.) Testimony that disregards the knowledge of a person of ordinary skill in the art cannot carry Mylan’s burden of proof by clear and convincing evidence. *See Capon v. Eshhar*, 418 F.3d 1349, 1357-59 (Fed. Cir. 2005) (vacating a finding of lack of written description support that failed “to consider the state of the scientific knowledge” because “[t]he ‘written description’ requirement must be applied in the context of the particular invention and the state of the knowledge”); *see also Zoltek Corp. v. United States*, 815 F.3d 1302, 1308 (Fed. Cir. 2016) (“The [written description] requirement is applied in the context of the state of knowledge at the time of the invention. The written description ‘need not include information that is already known and available to the experienced public.’”) (quoting

Space Sys/Loral, Inc. v. Lockheed Martin Corp., 405 F.3d 985, 987 (Fed. Cir. 2005) (citation omitted)).

D. Nuvo Does Not Support Mylan's Position

Mylan contends the Federal Circuit's decision in *Nuvo* is "highly instructive" and points to this decision in support of its written description argument. (Mylan Br. at 16.) Mylan's reliance is misplaced. *Nuvo*, which noted that the written-description inquiry is "highly fact specific," found lack of written description based on the facts in that case. 923 F.3d at 1383-84. In no respect did it change the basic principles of the written description law.

1. The Nuvo Decision

In *Nuvo*, the patent claims were directed to a novel pharmaceutical composition that included an acid inhibitor (e.g., a proton pump inhibitor ("PPI")) intended to reduce stomach acid and thus stomach upset associated with the use of NSAID pain medication. 923 F.3d at 1372-74, 1379. The acid inhibitor in the claimed formulation was only *partially* coated with an enteric coating to protect it from destruction by stomach acid. *Id.* at 1372-74. The composition also included an NSAID. *Id.* at 1372-73. The claims additionally required a certain measure of efficacy in reducing stomach acid, corresponding to a specific increased pH level: "an acid inhibitor present in an amount effective to raise the gastric pH of [a] patient to at least 3.5 . . ." *Id.* at 1372-73.

Importantly, the specification actually highlighted a known problem in the prior art with one component of the claimed formulation, namely that uncoated acid inhibitors (including PPIs) are *destroyed* by stomach acid and thereby rendered ineffective in reducing acid and raising pH. *Id.* at 1372-74. The specification even stated that "PPIs are 'enteric coated to avoid destruction by stomach acid.'" *Id.* at 1374 (quoting U.S. Patent No. 6,926,907, a patent-in-suit). In contradiction to this statement, the *Nuvo* patent claims were directed to compositions that included *uncoated* PPIs, and there was nothing in the specification to indicate that such compositions "could still be

effective to raise pH.” *Id.* at 1373-74. The Federal Circuit concluded that “[b]oth patents-in-suit . . . recite claims requiring amounts of uncoated PPI effective to raise the gastric pH to at least 3.5,” but that the patent specification did not provide written description support for that limitation given that the specification stated that PPIs are “enteric coated to avoid destruction by stomach acid.” *Id.* at 1373-74; *see also id.* at 1378, 1381.

Thus, *Nuvo* addresses a set of facts distinct from those here. In *Nuvo*, the Federal Circuit concluded that one of skill in the art would believe, as conceded by the patent specification, that one component of the claimed formulation would be “destr[oyed] by stomach acid” and thus would not work to achieve the claimed increase in pH. *Id.* at 1373-74. In contrast, there is no corresponding teaching in the ’514 patent cautioning against the claimed 480 mg/day dose or indicating it would not be effective. In fact, the ’514 patent specification teaches to the contrary: that the 480 mg/day dose is “effective” and links this dose to 720 mg/day, a known effective dose for treating MS. (*See* Wynn 476:12-17, 490:22-491:1, 491:8-15, 495:10-20.) In addition, there is no teaching in the prior art, even if it had any relevance here, that a 480 mg/day dose is ineffective. Indeed, Dr. Greenberg testified that he “did not come across studies where 480 milligrams had failed” (*See* Greenberg 429:12-24; *see also id.* at 185:21-24 (“I’m not aware of anything that would say” 480 milligrams would not work).)

Implicitly cautioning against the misapplication advanced by Mylan here, the *Nuvo* Court explained that its decision was highly fact-specific and based on the claims and specification at issue:

Written description analyses are *highly fact specific*. Based on the specific facts of certain cases, *it is unnecessary to prove that a claimed pharmaceutical compound actually achieves a certain result*. . . . In this case, the inventor chose to claim the therapeutic effectiveness of uncoated PPI, but he did not adequately describe the efficacy of uncoated PPI so as to demonstrate to ordinarily skilled

artisans that he possessed and actually invented what he claimed. And the evidence demonstrates that a person of ordinary skill in the art reading the specification would not have otherwise recognized, based on the disclosure of a formulation containing uncoated PPI, that it would be efficacious because he or she would not have expected uncoated PPI to raise gastric pH. Under those facts, the patent claims are invalid for lack of adequate written description pursuant to § 112, ¶ 1.

923 F.3d at 1383-84 (emphasis added) (citations omitted).

Nuvo therefore did not upset general principles relating to the interplay of obviousness and written description or introduce heightened requirements for establishing written description support. To the contrary, the *Nuvo* Court reaffirmed that the caselaw does not require “experimental data demonstrating effectiveness,” “theory or explanation of how or why a claimed composition will be effective,” or that the invention be actually “reduced to practice.” *Id.* at 1380.

2. Mylan Misapplies *Nuvo* To This Case

Mylan attempts to argue that the present case is like *Nuvo* by claiming, incorrectly, that Biogen and its experts have taken the position that “a POSA would not have expected [the 480 mg/day dose] to work *at all*.” (Mylan Br. at 14 (emphasis in original).) Mylan also relies on *Synthes USA, LLC v. Spinal Kinetics, Inc.*, 734 F.3d 1332 (Fed. Cir. 2013), in asserting that a “POSA’s expectations regarding the claimed efficacy of the 480 mg dose are also relevant to the written description analysis.” (Mylan Br. at 16.) *Synthes*, however, did not concern a skilled artisan’s expectations about whether the claimed invention would work.⁵ Moreover, Mylan again conflates obviousness (which relates to a POSA’s expectations based on the state of the art before the earliest patent filing date) and written description (which concerns the patent’s disclosure). As

⁵ In *Synthes*, the Court relied on the testimony of a skilled artisan—the defendants’ “research and development manager”—as supporting evidence of how a skilled artisan would understand a technical feature in the patent specification: whether “peripheral grooves” would be understood to serve the same function as “internal slots.” *Synthes*, 734 F.3d at 1342-43. Here, Mylan has not argued that any term in the ’514 patent specification has a meaning that is in dispute.

discussed above, the expectation of skilled artisans before reading the patent (based on the prior art) is a distinct question from whether a skilled artisan would understand after reading the patent that the specification describes the claimed invention (based on its written description).

Furthermore, Mylan has not identified any supporting evidence that “a POSA would not have expected [the 480 mg dose] to work at all.” (Mylan Br. at 14.) Mylan first points to Dr. Dawson’s statement in her declaration, relating to unexpected results, that “a person of ordinary skill in the art would not have a reasonable expectation that the 480 mg/day dose would provide statistically significant and clinically meaningful effectiveness for treating MS.” (Mylan Br. at 14.) This statement is not at all comparable to those in *Nuvo* that reflected a specific expectation, reflected in the patent specification itself, that one component of the claimed invention would fail to achieve the claimed, desired result. Moreover, Dr. Dawson’s declaration was focused on what the skilled artisan would understand *without* the benefit of the teachings of the ’514 patent. Dr. Dawson explained that, in light of the Phase II results, the Phase III results exhibited an unexpected magnitude of efficacy where the 480 mg/day dose “met all primary and secondary endpoints” including both MRI and clinical endpoints and did so “with a high level of statistical significance.” (JTX2088 at ¶ 12.)

There was no teaching in the prior art that a 480 mg/day dose was ineffective (*see* Greenberg 429:12-13 (“I did not come across studies where 480 milligrams had failed”)) and thus, in contrast to *Nuvo*, Dr. Dawson had no expectation that it would fail. As she explained in her trial testimony:

I think what we knew from [the Phase II study] was 720 milligrams per day showed an effect on MRI end points of disease that was statistically significant. That’s the information that we have. We know that 360 milligrams per day did not work. And somewhere in between that range of 360 to 720, there was the possibility that it

went from not working to working. So since 480 is a dose that's in between, it's possible it could work.

(Dawson 686:10-18.)⁶ And therefore, as Dr. Dawson explained, the 480 mg/day dose was chosen for testing in the Phase III study because “Dr. O’Neill had wanted to try 480 ever since I got to Biogen, which was in March 2004.” (*Id.* at 686:24-25.) According to Dr. O’Neill, he “believed from the outset that 480 milligrams as two divided doses of 240 milligrams per day would demonstrate efficacy.” (O’Neill 597:18-20.)

Mylan also quotes Biogen’s brief in the most recent inter partes review (“IPR”)⁷— *three* unsuccessful IPR challenges to the ’514 patent—that the skilled artisan viewing the known reports of Biogen’s Phase II studies, but without the benefit of the ’514 patent’s teachings, “would not have expected . . . 480 mg/day to be effective to treat MS.” (Mylan Br. at 14-15; D.I. 376-1 at 92 (Ex. B at 12).) But not having an expectation that a claimed invention will work, *based on the prior art*, is not akin to the facts of *Nuvo*, in which the Federal Circuit found that there was a specific expectation, stated in the specification itself, that one component of the claimed formulation would be destroyed in the stomach and thus could not work. Indeed, Mylan’s attempt to analogize to *Nuvo* cannot be correct, because if the skilled artisan would have expected 480 mg/day to be effective to treat MS based on the prior art (i.e., prior to reading the ’514 patent specification), then the claimed invention *would be obvious*. It is simply legally wrong to suggest

⁶ See also JTX2088 (Dawson Declaration) at ¶¶ 13-15 (explaining that “[t]he positive and clinically meaningful results . . . were unexpected . . . given (1) that the Phase 2 clinical trial indicated that both the 120 mg/day and 360 mg/day doses . . . were not efficacious and (2) that there was no apparent linear dose response”).

⁷ See D.I. 376-1 at 111-66 (*Mylan Pharms. Inc. v. Biogen MA Inc.*, IPR2018-01403, Paper No. 98 (Final Written Decision in favor of Biogen)); JTX2173 at 1005-33 (*Coalition For Affordable Drugs V LLC v. Biogen MA Inc.*, IPR2015-01993, Paper No. 63 (Final Written Decision in favor of Biogen)); see also *id.* at 988-1004 (*Coalition For Affordable Drugs V LLC v. Biogen MA Inc.*, IPR2015-01136, Paper 23 (Decision (denying institution of IPR))).

that all non-obvious inventions lack written description support. Furthermore, the quotation on which Mylan relies occurs in the context of a discussion of whether one of skill in the art would have expected a “clinical effect” that would be superior to existing MS drugs like Rebif®. (D.I. 376-1 at 91-92 (Ex. B. at 11-12) (“Biogen’s reported Phase II results provided no expectation that a clinical effect would occur below 720 mg/day Biogen’s 720 mg/day dose performed worse than Rebif® in MRI outcomes but ‘Rebif like’ for preliminary annualized relapse rates.”).) The ’514 patent claims do not require efficacy on clinical endpoints or superior efficacy to existing drugs. Rather, certain asserted patent claims require *therapeutic efficacy*, which the ’514 patent defines as including reduced neurodegeneration or inflammation, improvements that may be seen with MRI imaging as distinct from clinical measures. (JTX2000 at 5:52-59.)

Mylan also incorrectly suggests, by omitting words in a cropped quotation from Biogen’s IPR proceeding, that Biogen took the position that the patent claims require *clinical efficacy*: “Biogen distinguished prior art as purportedly failing to disclose ‘improvement for . . . any clinical measure.’” (Mylan Br. at 13.) The full statement, which responded to *Mylan’s* IPR argument about what the asserted Schimrigk 2004 reference allegedly discloses, points out that the reference “provided *no* further improvement for *Gd+ lesions* or any clinical measure.” (D.I. 376-1 at 30 (Mylan Ex. A at 21) (first emphasis in original, second emphasis added).) This full statement therefore does not state that clinical efficacy is required under the patent claims; the statement expressly refers to the non-clinical measure of Gd+ lesions,⁸ which are assessed via MRI.

⁸ “Gd+ lesions” are types of scars visible on certain MRI scans. “Upon administering Gd, gadolinium, contrast agent on a T1 [MRI] sequence you can see areas of active inflammation” in the brain. (Wynn 475:12-13; *see also id.* 475:7-9; 476:5-7 (“These are scars. Clearly one of our goals in treatment is to decrease the number of scars that people get in their brain.”).

Mylan is additionally incorrect in arguing that Dr. Wynn agreed that “the fact that the 480 mg dose ‘exhibited statistically significant efficacy at all was especially surprising.’” (Mylan Br. at 15 (citing Wynn 501:17-25, 502:8-23).) This statement was by counsel for Mylan, and Dr. Wynn did not simply agree to it. Rather, he explained that what was surprising to him was that the 480 mg/day dose exhibited statistically significant efficacy on “*clinical end points*.” (Wynn 502:8-13.) Thus, it was the “[t]he *magnitude* of this effect” in view of the state of the art as of the priority date was that was surprising. (*Id.* at 502:2-7 (emphasis added); *see also id.* at 501:3-5 (“It’s my opinion that, based upon the Phase 2 results, the *magnitude of treatment effect* that was seen in Phase 3 could not have been predicted.”) (emphasis added).) Dr. Wynn was surprised that 480 mg/day showed a statistically significant effect on “clinical end points” (*id.* at 502:13), which Dr. Wynn explained is a distinct and superior level of efficacy associated with Phase III clinical trials. (Wynn 531:3-14.) Certain of the patent claims require a “therapeutically effective amount,” a measure of efficacy that Dr. Wynn confirmed is “different than . . . clinical endpoints or clinically effective.” (Wynn 531:21-532:21 (“Q. Okay. Is that different than the clinical end points or clinically effective that we just discussed? A. Yes.”).) Therapeutic efficacy requires the “prevention or delay of onset or amelioration of symptoms of a neurological disorder in a subject or an attainment of a desired biological outcome such as reduced neurodegeneration, e.g., demyelination, axonal loss, and neuronal death, or reduced inflammation of the cells of the central nervous system.” (Wynn 531:21-532:6 (quoting JTX2000 at 5:52-59).) This broad definition includes results that are not clinical measures but may be observed “on [an] MRI scan.” (Wynn 531:21-532:7.) This measure of efficacy by MRI still constitutes a meaningful benefit to the patient because “the fewer scars one has in the brain as seen in MRI scan, the better it is.” (Wynn 532:16-19.)

Finally, Mylan incorrectly characterizes Dr. O'Neill's testimony, which is markedly different from that of the inventor in *Nuvo*. In *Nuvo*, the inventor testified that "he only had a 'general concept of coordinated delivery with acid inhibition' using uncoated PPI at the time he filed his patent application." *Nuvo*, 923 F.3d at 1381. Dr. O'Neill had far more than a "general concept"; he testified that he had a specific "belie[f] from the outset that 480 milligrams as two divided doses of 240 milligrams a day would demonstrate efficacy." (O'Neill 597:18-22.) Credible trial testimony corroborated this specific belief that Dr. O'Neill reiterated repeatedly from 2003 through the Phase III trials. (Lansden 662:17-663:8, 669:20-670:2, 677:5-13, 658:2-10; Bozic 366:4-9, 376:4-6; Dawson 682:21-683:7, 686:23-687:1.) Accordingly, in contrast to the inventor in *Nuvo*, Dr. O'Neill provided testimony, consistent with that of other witnesses, that corroborated his possession of the claimed invention described in the '514 patent specification. (O'Neill 558:15-559:4, 562:17-563:5, 571:21-25, 590:21-591:2.)

E. This Case is Also Unlike *Novozymes*

The present case is also unlike *Novozymes A/S v. Dupont Nutrition Biosciences APS*, 723 F.3d 1336 (Fed. Cir. 2013), which Mylan also cites. In *Novozymes*, the patent claimed a specific enzyme variant having a substitution at a particular amino acid position and possessing increased thermostability. *Id.* at 1341. The specification, however, "contain[ed] no disclosure of any variant that actually satisfie[d] the claims." *Id.* at 1348. Instead, the specification disclosed 7 parent enzymes of approximately 500 amino acid long enzyme chains, each having 33 target substitution positions, and at least 40 possible mutations at each target position. *Id.* at 1340. The *Novozymes* Court held that the specification failed to provide sufficient "blaze marks" that would guide one toward the specifically claimed combination among the "slew of competing possibilities." *Id.* at 1349. The court further emphasized that, to satisfy the written description requirement, the

application must describe the claimed subject matter “as an integrated whole rather than as a collection of independent limitations.” *Id.*

Here, in contrast, all elements of the claimed invention are explicitly disclosed with clear blaze marks and linked in the patent specification. The specification identifies in Method 4 a method of treating multiple sclerosis with an effective dose of DMF and/or MMF. (*See supra*, Section III.B.2-3.) And the specification further identifies 480 mg/day as an “effective dose” of DMF or MMF for oral administration. *Id.* The specification expresses a preference for all aspects of the claims, emphasizing the treatment of MS throughout the specification, focusing on DMF and MMF as compounds of interest and then disclosing the 480 mg/day dose in the narrowest, most preferred dose range, and linked to the known effective dose of 720 mg/day. *Id.* Thus, this case does not present the question raised in *Novozymes* of whether there were sufficient “blaze marks” that would lead one of skill in the art to the invention. Here the ’514 patent does much more than merely provide blaze marks for the skilled artisan—the invention is *specifically disclosed* and highlighted as preferred in the specification.

There is no requirement, as Mylan suggests (Mylan Br. at 21), that the three claim elements must be included in a single paragraph. *See Smith*, 481 F.2d at 914. As described in detail above, the specification provides a detailed and comprehensive description of the three related elements of the claimed treatment method. (*See supra*, Section III.B.2.)

Mylan is also incorrect in suggesting that Biogen “work[ed] backward” in its written description analysis. (Mylan Br. at 23.) A proper written description analysis starts with the claims. *In re Moore*, 439 F.2d 1232, 1235 (C.C.P.A. 1971) (“[I]t should be realized that when the first paragraph [of 35 U.S.C. § 112] speaks of ‘the invention,’ it can only be referring to that invention which the applicant wishes to have protected by the patent grant, i.e., the claimed

invention. For this reason, *the claims must be analyzed first* in order to determine exactly what subject matter they encompass.”) (emphasis added). Accordingly, Biogen’s expert Dr. Wynn began his written-description analysis by first explaining the subject matter encompassed by those claims and then identifying the explicit written description support. This analysis was not comparable to that in *Novozymes* where the specification “contain[ed] no disclosure of any variant that actually satisfies the claim,” 723 F.3d at 1348, and thus the patentee’s expert had to piece together the ““route one would travel through the forest of the specification to arrive at the claimed invention.”” *Id.* at 1349 (quoting *In re Ruschig*, 379 F.2d 990, 995 (C.C.P.A. 1967)).

Mylan asserts that a “POSA reading the specification would not have recognized 480 mg as a preferred dose for treating MS” (Mylan Br. at 21), incorrectly suggesting that under *Novozymes*, a specification must identify each aspect of a claimed invention as most preferred. *Novozymes* does not stand for that proposition, and written description law does not require that the specification single out 480 mg/day as the most preferred dose to describe the claimed invention, evident from Mylan’s failure to cite any supporting authority for this point. Rather, as the *Novozymes* Court explained, the specification must simply “describe an invention understandable to [a] skilled artisan and show that the inventor actually invented the invention claimed.” *Novozymes*, 723 F.3d at 1344 (quoting *Ariad* 598 F.3d at 1351). Mylan is also wrong that Dr. Wynn’s testimony supports its assertion that the patent does not identify 480 mg/day as a preferred dose. (Mylan Br. at 21 (citing Wynn 525:23-526:6).) Mylan overlooks Dr. Wynn’s explanation that, while the ’514 patent does not explicitly identify a *single* most preferred dose, it does identify a most preferred *range* of doses, 480-720 mg/day. (Wynn 532:24-533:4.) As Dr. Wynn further elaborated, the “inventors anchor 480 to a known effective dose of 720. And so I’m

directed to a lower range of the most narrow range in the nested ranges of doses in this patent. This patent teaches me to use 480.” (Wynn 526:24-527:3.)

Mylan also incorrectly argues that the possibility of inoperative embodiments (doses of DMF that did not reach the primary endpoint in the Phase II trial) negates written description support for the claimed invention or would cause the skilled artisan not to recognize the disclosure of the claimed invention. (Mylan Br. at 21-22). That is not the law. *Snitzer v. Etzel*, 465 F.2d 899, 902 (C.C.P.A. 1972). The fact that the ’514 patent specification describes unclaimed lower doses of DMF and/or MMF that may be ineffective to treat MS is irrelevant to the determination of whether the specification provides written description support for the claimed 480 mg/day dose of DMF and/or MMF to treat MS. *See Snitzer*, 465 F.2d at 902 (“[W]e fail to see the relevance of the listing of several inoperative species when the species claimed is operative . . .”). The ’514 patent specification describes 480 mg/day as an “effective” dose of DMF for treating MS, further discloses 480 mg/day as the lowest endpoint in “the most preferred range of the listed ranges” of doses for oral administration of DMF and/or MMF (Wynn 532:25-533:6; *see also id.* 490:19-25) and links that dose to a known effective dose, 720 mg/day. (Wynn 495:14-20 (explaining the “progressively narrowing ranges, nesting ranges, leading one to the most narrow range, 480 to 720, . . . and anchoring to a known effective dose of 720, . . . 480 being the lower end of the range, teaching me that 480 would be an effective dose for oral administration of dimethyl fumarate or monomethyl fumarate to someone with multiple sclerosis.”).) The specification thus provides explicit and unequivocal written description support for the claimed invention.

IV. CONCLUSION

The ’514 patent specification describes to skilled artisans all elements of the claimed inventions as an integrated whole, and Mylan’s repeated efforts to improperly conflate the issues of obviousness and written description should be rejected. Likewise, Mylan’s misapplication of

the *Nuvo*, *Synthes*, and *Novozymes* cases should be rejected. Finally, Mylan's "repurposing" rhetoric is both unsupported by the record and legally irrelevant to the written description inquiry. For the reasons explained herein and at trial, Mylan has not carried its heavy burden of proving by clear and convincing evidence that the asserted '514 patent claims are invalid for lack of written description and judgment should enter against Mylan.

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CERTIFICATE OF SERVICE

I hereby certify that on April 3, 2020, I caused a true and correct copy of the foregoing BIOGEN'S RESPONSIVE POST-TRIAL BRIEF to be electronically filed with the Clerk of the Court using the CM/ECF system, and have served a true and correct copy via email on the below counsel of record.

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